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Gastroesophageal reflux disease and laparoscopic sleeve gastrectomy: a physiopathologic evaluation

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Structured abstract

Objectives: To evaluate the effect of laparoscopic sleeve gastrectomy (LSG) on gastroesophageal reflux disease (GERD) in morbidly obese patients.

Background data: Symptomatic GERD is considered by many a contraindication to LSG. However, studies evaluating the relationship between LSG and GERD by 24-hour pH monitoring are lacking.

Methods: Consecutive morbidly obese patients selected for LSG were included in a prospective clinical study. Gastroesophageal function was evaluated using a clinical validated questionnaire, upper endoscopy, esophageal manometry and 24-hour pH monitoring before and 24 months after LSG. This trial is registered with ClinicalTrials.gov, number NCT02012894.

Results: From June 2009 to September 2011, 71 patients entered the study; 65 (91.5%) completed the 2-year protocol. Based on the preoperative 24-hour pH monitoring, patients were divided into group A (pathologic, n=28) and group B (normal, n=37). Symptoms improved in group A, with the Gastroesophageal reflux disease Symptom Assessment Scale score decreasing from 53.1 ± 10.5 to 13.1 ± 3.5 ($p < 0.001$). DeMeester's score (DMS) and total acid exposure (% pH<4) decreased in group A patients (DMS from 39.5 ± 16.5 to 10.6 ± 5.8 , $p < 0.001$; % pH<4 from 10.2 ± 3.7 to 4.2 ± 2.6 , $p < 0.001$). Real "de novo" GERD occurred in 5.4% group B patients. No significant changes in lower esophageal sphincter pressure and esophageal peristalsis amplitude were found in both groups.

Conclusion: LSG improves symptoms and controls reflux in most morbidly obese patients with preoperative GERD. In obese patients without preoperative evidence of GERD, the occurrence of “de novo” reflux is uncommon. Therefore LSG should be considered an option for the surgical treatment of obese patients with GERD.

Keywords: obesity – gastroesophageal reflux – laparoscopic sleeve gastrectomy – 24-hour pH monitoring.

Mini-abstract

Laparoscopic sleeve gastrectomy improves symptoms and controls reflux in most morbid obese patients with preoperative pathologic gastroesophageal reflux. The postoperative occurrence of “de novo” reflux in patients without preoperative evidence of GERD is uncommon.

INTRODUCTION

Gastroesophageal reflux disease (GERD) is frequently associated with morbid obesity.¹ Several studies have investigated the impact of bariatric procedures, such as laparoscopic adjustable silicone gastric banding,²⁻⁴ vertical banded gastroplasty,^{2,4,5} and Roux-en-Y gastric bypass (LRYGB),⁶⁻⁹ on GERD symptoms and esophageal function. RYGB is considered by many the most effective surgical procedure in the treatment of morbid obese patients with GERD.¹⁰

More recently, laparoscopic sleeve gastrectomy (LSG) has been proven to be an effective weight loss procedure and has gained wide acceptance as standalone surgical option for the treatment of morbid obesity.¹¹⁻¹⁴ It is technically easier and is associated with lower postoperative morbidity and mortality rates than LRYGB.¹⁵

Data concerning the effects of LSG on esophageal function and GERD are limited and controversial. Symptomatic GERD is considered by many a contraindication to LSG. However, several heterogeneous studies have investigated the outcomes of LSG in terms of GERD control, with the majority reporting only changes in symptoms and manometric findings, without an objective evaluation of gastroesophageal reflux with ambulatory 24-hour pH monitoring.^{11,12,14,16-29}

The aim of this prospective study was to objectively evaluate the effects of LSG on GERD and esophageal function in morbidly obese patients.

METHODS

The study population consisted of consecutive morbidly obese patients eligible for LSG. All patients fulfilled the 1991 National Institute of Health (NIH) criteria for bariatric surgery.³⁰

Exclusion criteria were the presence of large hiatal hernia (any hiatal hernia with more than half of the stomach herniated into the chest), and previous gastric surgery. Preoperative work-up included clinical examination, upper endoscopy, barium swallow, stationary esophageal manometry, and 24-hour pH monitoring.

Patient characteristics were entered into a prospective database including preoperative assessment, intraoperative data, early postoperative results, and clinical and functional outcomes at 24 months after surgery. Gastroesophageal function was evaluated using a clinically validated questionnaire, the Gastroesophageal reflux disease Symptom Assessment Scale (GSAS),^{31,32} esophageal manometry and 24-hour pH monitoring. The protocol was approved by the ethical committee of our institution, and patients gave informed consent.

Upper endoscopy

Upper endoscopy was obtained in all patients preoperatively. Findings of hiatal hernia were recorded and esophagitis was described in detail according to the Savary-Miller classification.³³ Biopsies were routinely taken at the gastroesophageal junction, and in the stomach to rule out a *Helicobacter pylori* (HP) infection. In case of HP infection, amoxicillin-clarithromycin-containing triple therapy was administered.

Barium swallow

A radiological study of the upper gastrointestinal tract was performed using a low-density barium sulfate suspension. The following parameters were evaluated: 1) the presence of short esophagus; and 2) the presence, type and size of a hiatal hernia.

Esophageal manometry

Stationary esophageal manometry was performed using a 8-channel perfusion catheter as described previously.³⁴

Twenty-four-hour pH monitoring

Twenty-four-hour pH monitoring was performed using a combined glass pH electrode and a digital data logger (pH-day 2 portable unit, Menfis Biomedica, Bologna, Italy) as described elsewhere.³⁵

Data were analysed using a pH-monitoring dedicated software (pH/HS Menfis Biomedica, Bologna, Italy). Gastroesophageal reflux was assessed using the DeMeester's composite reflux score (DMS)

and total acid exposure (%pH<4).³⁶ Esophageal acid clearance and the symptom index (SI) were also calculated. Symptom episodes were defined as reflux-related if the SI was higher than 50%.³⁷

Surgical technique

Five 10-mm trocars were used for the procedure. Starting from a point midway along the greater curvature of the stomach, the greater sac was entered and the short gastric vessels were taken down using an electrothermal bipolar vessels sealing device. The short gastric vessels division was performed proximally all the way up to the angle of His, and distally 6 cm proximal to the pylorus. Hiatoptasty in presence of small hiatal hernia was not routinely performed. A 36-Fr bougie was then inserted trans-orally under laparoscopic vision down to the pyloric channel along the lesser curvature of the stomach. An endoscopic linear stapler was used to longitudinally transect the stomach just lateral to the bougie up to the gastroesophageal junction, with particular attention to perform a regular shape of the sleeve and to avoid inclusion of the sling fibers of Helvetius in the resected specimen. The staple line was then checked for bleeding and tested for leak with the methylene blue test. A drain was placed along the staple line. The resected portion of stomach was then placed in a specimen bag and removed through the supraumbilical trocar site.

On the first or second postoperative day, upper gastrointestinal radiological series with water soluble solution were obtained in all patients to evaluate the residual gastric volume and to rule out postoperative leaks, before starting oral intake.

Outcome Assessment

Gastroesophageal function was assessed by GSAS, upper endoscopy, esophageal manometry and ambulatory 24-hour pH monitoring at 24 months after LSG.

The primary end point was the effect of LSG on esophageal acid exposure in morbidly obese patients at 24-hour pH monitoring. The secondary end points were 1) the occurrence of reflux symptoms and 2) manometric changes at 24-month follow-up.

Statistical Analysis

Quantitative data are given as mean and standard deviation, and categorical data are expressed as percentages. The chi-square test was used to compare proportions. The Student's *t* test was used to compare normally distributed variables. Functional data obtained from 24-hour pH monitoring and esophageal manometry, and the scores derived from patient responses to GSAS questionnaire items were used to define changes in postoperative function.

A stepwise logistic regression analysis was performed to identify predictors of postoperative pathological reflux. The variables potentially related to postoperative reflux with $P \leq 0.200$ in the univariate analysis were entered into a multivariate analysis. The predictor variables considered were patient age, postoperative Body Mass Index (BMI) (calculated as weight in kilograms divided by height in meters squared), excess weight loss percentage (EWL%), preoperative pathologic acid exposure, preoperative hypotensive lower esophageal sphincter (LES), and presence of hiatal hernia. Results are reported as odds ratio with 95% confidence intervals.

All *p* values were two-sided. A level of 5% was set as the criterion for statistical significance. The data were collected on an Excel spreadsheet. The statistical analysis was performed using SPSS version 19 (Copyright © SPSS Inc., 2000). This trial is registered with ClinicalTrials.gov, number NCT02012894.

RESULTS

From June 2009 to September 2011, 106 morbidly obese patients underwent LSG. Of these, 35 patients were excluded from the study: 16 refused to undergo the follow-up protocol, 14 had previous gastric surgery, and 5 had large hiatal hernia treated with LRYGB and hiatal repair in all cases. The remaining 71 morbidly obese patients entered the study (Fig. 1); 6 patients (8.5%) were men and 65 (91.5%) were women. Mean age was 42.6 ± 10.2 years and the BMI was 44.3 ± 3.8 kg/m².

Patients were divided into 2 groups according to the preoperative 24-hour pH monitoring: 30 patients (42.3%) with pathologic esophageal acid exposure (group A) and 41 (57.7%) with normal acid exposure (group B). No significant differences were observed in age, sex distribution, and BMI between group A and B. The preoperative GSAS score and prevalence of symptoms in each group are reported in Table 1.

Before surgery, HP infection was diagnosed in 4 group A patients (13.3%) and in 3 group B patients (7.3%) and eradicated with amoxicillin-clarithromycin-containing triple therapy in all patients. All group A and 8 (19.5%) group B patients were receiving proton pump inhibitor (PPI) therapy before surgery. An adequate symptom control on PPIs was obtained in 28 (93.3%) group A patients with early recurrence of symptoms when PPI therapy was discontinued.

The mean operative time of LSG was 81.8 ± 21.2 minutes with no conversion to open surgery. There was no mortality; the morbidity rate was 2.8%, including 2 patients (one in each group) undergoing blood transfusion for bleeding on the second postoperative day.

At hospital discharge, all patients were instructed to consume a semiliquid diet and received PPI therapy (30 mg/day for the first 30 days and 15 mg/day for the subsequent 3 months).

Two (6.7%) group A patients and 4 (9.8%) group B patients were lost to follow-up. Therefore, 65 (91.5%) patients completed the 2-year protocol and were included in the analysis: 28 patients in the group A and 37 in the group B. The BMI had decreased to 31.5 ± 5.3 Kg/m² with 54% EWL% in group A, and to 30.6 ± 4.8 Kg/m² with 56% EWL% in group B ($P=0.477$).

At 2-year follow-up, upper endoscopy revealed esophagitis in 2/28 (7.1%) group A patients (2 grade II) and in 3/37 (8.1%) group B patients (1 grade I and 2 grade II) ($P=0.745$), without esophageal metaplasia. Dilatation of the upper portion of the sleeve was found in 5 (13.5%) group B patients. A barium swallow obtained in these patients confirmed this endoscopic finding with decreased gastric emptying at level of the midstomach.

Functional Results

The preoperative and postoperative data obtained with the stationary esophageal manometry are summarized in Table 2. No significant differences were observed between preoperative and postoperative manometric data in each group.

In group A, 24-hour pH monitoring showed a significant decrease in both DMS and total %pH<4 at 2-year follow-up compared with baseline values (Table 2). Pathologic esophageal acid exposure was reduced but still present in 4 (14.3%) patients. The mean SI score was significantly lower at 24 months compared with the preoperative value (84.8 ± 6.2 vs. 15.4 ± 4.3 , $P < 0.001$). The rate of patients with SI greater than 50% decreased from 89.3% (n=25) preoperatively to 14.3% (n=4) at 24 months ($P < 0.001$).

In group B, DMS and total %pH<4 did not significantly change at 2 years after surgery (Table 2). Pathological DMS and total %pH<4 were observed in 7 (18.9%) patients, with the esophageal acid exposure predominantly postprandial in 5 of them.

The mean SI score was not significantly different at 24-month follow-up compared with the preoperative value (32.5 ± 8.7 vs. 33.8 ± 3.2 , $P = 0.396$). Overall, the percentage of patients with SI of more than 50% slightly increased from 8.1% (n=3) preoperatively to 18.9% (n=7) at 24 months ($P = 0.308$).

Clinical Results

In group A, symptoms significantly improved during the follow-up period with the GSAS score decreasing from 53.1 ± 10.5 to 13.1 ± 3.5 ($P < 0.001$). Four (14.3%) patients experienced episodes of heartburn and acid regurgitation that were well controlled by acid reducing medications.

In group B, the mean GSAS score decreased from 45.8 ± 9.6 to 31.7 ± 15.9 ($P < 0.001$). Two of the 7 patients with “de novo” postoperative pathological 24-hour pH monitoring reported symptoms suggestive for GERD predominantly in the supine position; the mean GSAS score increased from 34.7 to 47.1. Symptoms were well controlled with PPI in both patients.

The other 5 patients presented a midstomach stenosis and experienced symptoms suggestive for GERD predominantly in the postprandial period that were associated with dysphagia and gas bloating. An increase from 35.5 to 46.4 in the mean GSAS score was observed. Mean EWL% in these 5 patients was 75.4%. A partial control of symptoms has been achieved with PPIs and prokinetics in association with a soft diet.

Univariate analysis showed that EWL% greater than 70% and preoperative pathological reflux at 24-hour pH monitoring were the factors significantly associated with pathological reflux after LSG. On multivariate analysis, no factor was found as significant predictor of pathological reflux (Table 3).

DISCUSSION

The relationship between LSG and GERD is multifactorial and the effects of LSG on gastroesophageal function are unclear. While some studies have shown increased prevalence of GERD after LSG,^{11,18-23,27} others have reported improvement of reflux postoperatively.^{12,16,17,24} Several anatomic factors and physiologic mechanisms have been proposed to explain the increased prevalence of GERD after LSG: hypotensive LES, disruption of the angle of His, resection of sling fibers, reduced gastric compliance with higher intragastric pressure, decreased gastric emptying, late dilatation of the sleeve and occurrence of hiatal hernia. On the contrary, factors associated with reduced GERD after LSG include weight loss, restoration of the angle of His, decreased acid production, and accelerated gastric emptying.

The studies investigating GERD and esophageal function after LSG are heterogeneous and most of them have reported symptom evaluation only, without objective assessment of reflux using ambulatory 24-hour pH monitoring. Even though the evidence available is limited, GERD is considered by many a contraindication to LSG. LRYGB is widely considered the procedure of choice for the surgical treatment of GERD in morbid obese patients. However, it is a more complex procedure and it is associated with a higher incidence of postoperative complications than LSG.³⁸

This is the first prospective study aiming to assess objectively the impact of LSG on esophageal acid exposure in morbid obese patients with preoperative GERD, and the development of “de novo” postoperative GERD. Patients with a giant hiatal hernia were excluded from the study. The management of giant hiatal hernia in morbidly obese patients is a therapeutic challenge. Both LSG and LRYGB combined with hiatal repair have been suggested as good options for the treatment of selected patients.³⁹⁻⁴² However, in the absence of comparative studies, the ideal surgical procedure that addresses both obesity and giant hiatal hernia has not been well established. In the group of patients with preoperative GERD, the 24-hour pH monitoring at 2 years demonstrated a significant decrease in both DMS and total %pH<4. These findings were associated with significantly better GSAS score and lower esophagitis rate after surgery. In the absence of

specific studies, we hypothesize that the decreased acid production secondary to the reduced number of parietal cells, and the absence of midstomach stenosis demonstrated at the upper endoscopy may have a positive impact on the esophageal acid exposure.

In group B, the 24-hour pH monitoring detected in 7 (18.9%) patients “de novo” pathologic esophageal acid exposure, that was predominantly postprandial in 5 of them. These 5 patients experienced symptoms suggestive for GERD in addition to obstructive symptoms, such as dysphagia and gas bloating, associated with a significantly higher EWL%. Upper endoscopy and barium swallow demonstrated dilatation of the upper portion of the sleeve. The other two patients with postoperative pathological 24-hour pH monitoring reported only symptoms suggestive for GERD predominantly in the supine position, well controlled by acid reducing medications.

The reported increase in postoperative “de novo” GERD prevalence based on symptoms evaluation ranges between 2.1%¹⁹ and 23%¹¹ and proximal sleeve dilatation (“neofundus”) has been proposed as possible predisposing factor. For instance, Himpens et al.¹¹ reported the long-term outcomes in 30 patients undergoing stand alone LSG for morbid obesity. Patients were contacted by phone after the sixth postoperative year and were invited to fill out a questionnaire including GERD symptom evaluation. The authors found a 23% incidence of GERD symptoms. However, the interpretation of these data is limited by the lack of objective evaluation of GERD by 24-hour pH monitoring. We observed GERD symptoms in all patients with postoperative pathologic esophageal acid exposure. However, a careful analysis of symptoms and their correlation with the 24-hour pH monitoring data suggest that real “de novo” GERD occurred in 5.4% (2/37) patients, while the pH decrease below 4 was secondary to food stasis in the upper portion of the sleeve causing symptoms simulating “de novo” GERD in 13.5% (5/37) patients.

Our results show rates of persistent postoperative GERD and new-onset GERD similar to those reported after LRYGB,⁴³ with symptoms being well controlled with PPI.

The surgical technique might play a major role in reducing the risk of postoperative GERD^{29,44,45}. In this regard, two technical aspects are critical: gastric resection without creating a mid-stomach

stenosis and careful dissection of the angle of His maintaining a safe distance from the gastro-esophageal junction.

Data regarding manometric changes after LSG are controversial. Braghetto et al.⁴⁶ demonstrated a significant postoperative reduction in LES pressure in 85% of patients at 6-month follow-up after LSG, and they correlated this finding with partial section of the sling fibers of the cardia. Conversely, Kleidi et al.²⁶ evaluated the effects of LSG on the LES function and GERD symptoms in 23 obese asymptomatic patients. All patients underwent esophageal manometry and symptom evaluation preoperatively and at least 6 weeks postoperatively. They observed a significant increase in LES total and abdominal length and pressure, and reduced peristalsis amplitude in the lower esophagus. Petersen et al.²⁵ reported increased LES pressure regardless of the weight loss and concluded that the observed manometric changes were related to the surgical technique.

We did not observe significant differences in LES length, LES pressure and distal esophageal waves amplitude at the postoperative esophageal manometry compared with the baseline values in both groups of patients. These results suggest that LSG *per se* might not adversely affect the LES and esophageal function and highlight the importance of surgical technique.

Conclusions

In obese patients affected by GERD, LSG improves symptoms and controls reflux in most cases, while in patients without preoperative evidence of GERD, the occurrence of “de novo” reflux is uncommon. Therefore, LSG should be considered an option for the surgical treatment of obese patients with GERD.

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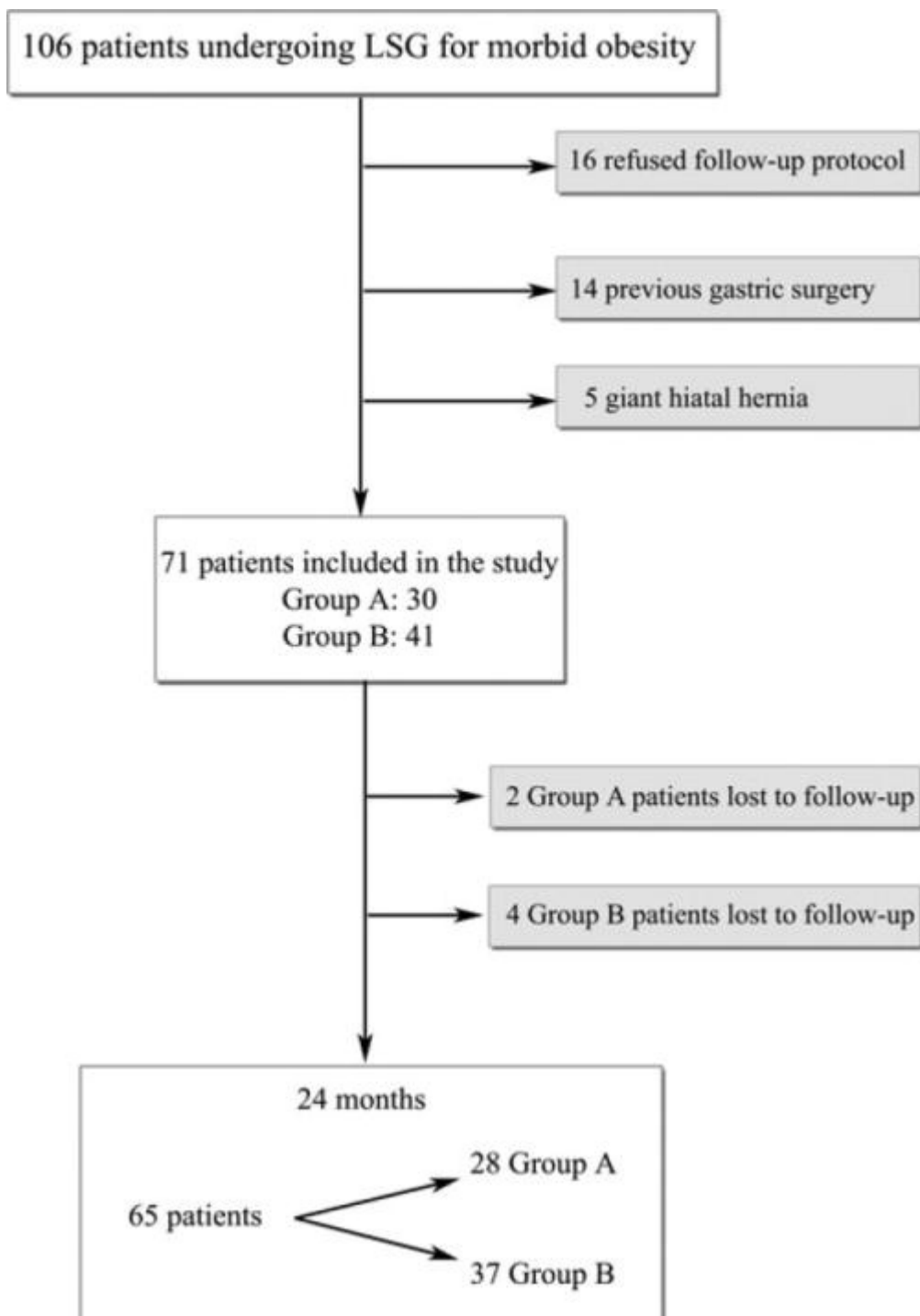
Figure 1

Table 1

	Group A (N = 30)	Group B (N = 41)	P
Age, yr	41.8 ± 9.8	43.1 ± 10.5	0.598
Sex (females), n (%)	27 (90)	38 (92.7)	0.976
BMI, kg/m ²	44.2 ± 3.6	44.4 ± 3.9	0.826
Comorbidity, n (%)			
Hypertension	11 (36.7)	16 (39)	0.964
Type II diabetes	5 (16.7)	7 (17.1)	0.783
OSAS	3 (10)	4 (9.8)	0.712
Symptoms, n (%)			
Heartburn	22 (73.3)	3 (7.3)	<0.001
Regurgitation	24 (80)	4 (9.8)	<0.001
Hoarseness	8 (26.7)	2 (4.9)	0.024
Cough	10 (33.3)	0	<0.001
Gas-bloating	5 (16.7)	26 (63.4)	<0.001
Flatulence	11 (36.7)	31 (75.6)	0.002
GSAS score	52.5 ± 10.1	44.9 ± 7.5	0.001
Upper endoscopy			
Esophagitis, n (%)	6 (20)	3 (7.3)	0.220
Grade I	2	2	
Grade II	3	1	
Grade III	1	0	
Small hiatal hernia	5 (16.7)	3 (7.3)	0.395
Barium swallow			
Small hiatal hernia, n (%)	7 (23.3)	4 (9.8)	0.219
Sliding	7 (100)	4 (100)	

Values are given as mean ± standard deviation unless indicated otherwise.
OSAS indicates obstructive sleep apnea syndrome.

Table 2

Variable	N	Univariate Analysis		Multivariate Analysis	
		Odds Ratio	P	Odds Ratio	P
Age, yr					
≤42	32	1	0.976		
>42	33	1.02 (0.44–1.21)			
Postoperative BMI, kg/m ²					
<31	33	1	0.532		
≥31	32	1.77 (0.81–3.77)			
EWL%					
<70	59	1	0.040	1	0.411
≥70	6	2.13 (1.15–2.39)		1.67 (0.82–3.25)	
Preoperative pathologic acid exposure					
No	28	1	0.041	1	0.332
Yes	37	2.05 (1.12–6.02)		1.79 (0.76–4.14)	
Preoperative hypotensive LES					
No	40	1	0.340		
Yes	25	2.21 (0.66–4.52)			
Hiatal hernia					
No	54	1	0.661		
Yes	11	1.47 (0.41–1.71)			

Values in parentheses are 95% confidence intervals.

Table 3

Variable	N	Univariate Analysis		Multivariate Analysis	
		Odds Ratio	P	Odds Ratio	P
Age, yr					
≤42	32	1	0.976		
>42	33	1.02 (0.44–1.21)			
Postoperative BMI, kg/m ²					
<31	33	1	0.532		
≥31	32	1.77 (0.81–3.77)			
EWL%					
<70	59	1	0.040	1	0.411
≥70	6	2.13 (1.15–2.39)		1.67 (0.82–3.25)	
Preoperative pathologic acid exposure					
No	28	1	0.041	1	0.332
Yes	37	2.05 (1.12–6.02)		1.79 (0.76–4.14)	
Preoperative hypotensive LES					
No	40	1	0.340		
Yes	25	2.21 (0.66–4.52)			
Hiatal hernia					
No	54	1	0.661		
Yes	11	1.47 (0.41–1.71)			

Values in parentheses are 95% confidence intervals.